their incidence and risk-factors following fludarabine (F)-based RIC and RTC has not been well defined, due to still limited follow-up after these novel regimens. We retrospectively reviewed data of 931 patients (pts) given allogeneic SCT over a 12 year period to identify pts with secondary malignancies. Conditioning regimens included standard MAC (n = 257, TBI-based in 111), F-based RIC [n = 449, including F with intermediate-dose busulfan, (FB2), and F with melphalan (FM)] or F-based RTC [n = 225, including F with high-dose busulfan, (FB4), and F with treosulfan (FT)]. 21 pts had secondary malignancies including squamous cell carcinoma of the skin (n = 5), penis (n = 1) vagina (n = 1), tongue (n = 1) and esophagus (n = 2), colon cancer (n = 3), breast cancer (n = 2), pancreatic cancer (n = 2), metastatic cancer of unknown primary (n = 1), melanoma (n = 1), metastatic sarcoma (n = 1), Kaposi sarcoma (n = 1). In all, 5 pts had metastatic or locally advanced solid tumor at presentation. The median age at SCT was 53 years (29-70). 19 pts were given F-based RIC/RTC and none had TBI. The median time from SCT to diagnosis of second malignancy was 49 months (7 months-11.5 years). 17 pts had prior cGVHD, 10 moderate-severe and 14 were still on immunosuppressive therapy at the diagnosis of secondary malignancy. The 10-year cumulative incidence of secondary malignancy was 5.3% (95%CI, 3.2-8.7%). It was 2.2% after BuCy, 8.8% after FB2, 5.5% after FM, 7.8% after FB4 and 5.5% after FT (p = 0.05 for BuCy Vs. RIC/RTC). Multivariate analysis identified RIC/RTC and moderate-severe cGVHD as adverse prognostic factors, HR 5.9 (p = 0.03) and 2.7 (p = 0.04), respectively. Pts were treated with surgery for localized tumors and with chemo-radiotherapy or palliative therapy for metastatic disease. Currently, 17 pts are alive and 4 died, all of them had advanced solid tumor at presentation. The cumulative incidence of death due to secondary malignancy was 1.6% at 10 years after SCT. In conclusion, secondary malignancies are rare but significant complication after allogeneic SCT. Curative approach is feasible in a subset of pts. The combination of F and intermediate to high-dose alkylating agent may be associated with higher risk for second malignancies than standard therapy with high-dose alkylators and/or TBI. Larger registry studies with more events are needed to confirm these observations.

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LONG-TERM FOLLOW-UP OF HEMATOPOIETIC CELL TRANSPLANT (HCT) RECIPIENTS AFTER RSV PNEUMONIA

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Background: Respiratory syncytial virus (RSV) infection can cause severe pneumonia after HCT. Although there are many reports about early clinical outcomes after RSV pneumonia, late sequelae are less well characterized. Therefore, we investigated the late pulmonary function effects of RSV pneumonia after HCT.

Patients and Methods: HCT recipients who had RSV pneumonia (radiographic signs and BAL positive for RSV by PCR, DFA or culture) between 1/1990 and 3/2010 and survived for at least 1 month were retrospectively reviewed. Patients who had pulmonary function tests (PFTs) at the time of both pre- and post- (day 60±25 and/or 1 year±80 days) RSV pneumonia were analyzed. Airflow obstruction was defined as FEV1/FVC<0.7, FEV1≤75%, and FEV1 decrease of ≥10% according to the modified NIH guidelines. All patients received aerosolized ribavirin (RBV) +/- palivizumab.

Results: A total of 28 patients had RSV pneumonia a median of 29.5 days after HCT (range, 9- 1515 days) and survived for at least 1 month. Median patient age was 37 years (range, 10- 67); 27/28 were allograft recipients. Survival at 100 days and 1 year after RSV pneumonia was 89.3% and 78.6%, respectively; all deaths were unrelated to RSV (5 died of non-respiratory causes and one with respiratory failure due to bronchiolitis obliterans). PFTs at day 60 showed significant decreases of %FEV1 and %DLCO compared with before RSV pneumonia (−9.5%±13.0, $p = 0.003$, −24.0%±18.2, $p < 0.001$, respectively). Pulmonary function at 1 year after RSV pneumonia was also significantly decreased when compared to baseline (%FEV1: −6.9%±12.0, $p = 0.049$, %DLCO: −16.7%±21.2, $p = 0.01$) but not significantly improved compared with day 60 measurements. Seventeen patients received palivizumab in addition to aerosolized RBV in a non-randomized fashion (there were no significant differences in patient age, acute and chronic GVHD, or pretransplant PFTs between patients who did and did not receive palivizumab). Analysis stratified by palivizumab use did not significantly affect the PFT observations. Airflow obstruction at 1 year post RSV pneumonia was detected in 4 of 16 patients. Palivizumab use did not affect the incidence of airflow obstruction (20% with palivizumab and 33% without, $p = 0.6$).

Conclusions: Long term survivors of RSV pneumonia after HCT may be at risk for persistent airflow abnormalities. The addition of palivizumab did not appear to improve late pulmonary function in this relatively small retrospective study.

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LATE MORTALITY AFTER HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR A CHILDHOOD MALIGNANCY

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Hematopoietic stem cell transplantation (HSCT) is used increasingly as a curative therapy in children with malignancies. However, survivors of HSCT are at risk for disease recurrence and life-threatening complications. The risk for late mortality (>2 years) after autologous and allogeneic HSCT has not been well reported in children. The aim of this population-based retrospective cohort study was to assess late mortality in children (age 0-18 y-o) who underwent a HSCT in the province of Ontario, Canada. Nearly all of the province's pediatric transplantations are performed at a single center (SickKids). Indication for HSCT, type of transplant, donor source and survival were determined via a record linkage between the SickKids' transplant database and POGONIS, the provincial pediatric cancer registry. Mortality information contained in POGONIS is captured at the time of death in hospital, or by record linkage to the provincial mortality file. Records of all 756 children who were Ontario residents with a malignancy and underwent HSCT at SickKids between 1985-2009 were retrieved. Underlying diagnoses were leukemia (N = 412), lymphoma (N = 82), CNS tumor (N = 55), neuroblastoma (N = 150), sarcoma (N = 41) and other (N = 16). 372 children underwent allogeneic HSCT and 384 underwent autologous HSCT. Among the allogeneic HSCT group, 226 (60.8%) received related donor HSCT. Overall, 479 children (63.4%) survived for at least 2 years after HSCT. The median follow-up of these 479 survivors was 9.98 years. Of these 479 survivors, 98 (20.5%) subsequently suffered a late death. A greater proportion of patients who underwent autologous HSCT had a late death (64/251; 25.5%) than patients post allogeneic HSCT (34/228; 14.9%). In a multivariate analysis of patients who underwent autologous HSCT, males had increased risk of death compared to females (HR = 2.0, 95% CI:1.12-3.59), and patients treated for neuroblastoma had a greater risk of death than those treated for leukemia (HR = 10.0, 95% CI:2.78-36.2). Among patients treated with allogeneic HSCT, none of gender, donor source (related vs. unrelated), age at transplant or underlying diagnosis was associated with increased late mortality.

In conclusion, children with cancer who are treated with a HSCT continue to be at risk for premature death even if they survive for 2 or more years after their transplant. Further investigation will focus on examining the contributions of treatment toxicity and disease recurrence to late mortality.